THE EFFECT OF ORAL METHYLPREDNISOLONE PULSE ON BLOOD SUGAR

DISSERTATION SUBMITTED IN FULFILLMENT OF THE REGULATIONS FOR THE AWARD OF

M.D. DERMATOLOGY, VENEREOLOGY & LEPROSY

DEPARTMENT OF DERMATOLOGY, VENEREOLOGY & LEPROSY

PSG INSTITUTE OF MEDICAL SCIENCES & RESEARCH

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

GUINDY, CHENNAI, TAMILNADU, INDIA

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GUIDE

DR. C.R.SRINIVAS, MD.,

DEPARTMENT OF DERMATOLOGY, VENEREOLOGY & LEPROSY

PSG INSTITUTE OF MEDICAL SCIENCES & RESEARCH

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Certificate

CERTIFICATE

This is to certify that the thesis entitled "**THE EFFECT OF ORAL METHYLPREDNISOLONE PULSE ON BLOOD SUGAR**" is a bonafide work of **Dr M. Barathi** done under my direct guidance and supervision in the Department of Dermatology, Venereology and Leprosy, PSG Institute of Medical Sciences and Research, Coimbatore in fulfillment of the regulations of Dr .MGR Medical university for the award of MD degree in Dermatology, Venereology and Leprosy.

GUIDE & HOD PRINCIPAL

DECLARATION

I hereby declare that this dissertation entitled "**THE EFFECT OF ORAL METHYLPREDNISOLONE PULSE ON BLOOD SUGAR**" was prepared by me under the direct guidance and supervision of **Prof. Dr. C.R.SRINIVAS MD.,** PSG Hospitals, Coimbatore.

The dissertation is submitted to the Dr. M.G.R. Medical University in partial fulfillment of the University regulations for the award of MD degree in Dermatology, Venereology and Leprosy. This dissertation has not been submitted for the award of any Degree or Diploma.

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Introduction

INTRODUCTION

Systemic corticosteroids are one of the commonly prescribed drugs for dermatological conditions. Conventional corticosteroids was associated with many side effects like hypertension, hyperglycemia, eye changes like cataract, glaucoma, bone changes like osteoporosis, avascular necrosis. Corticosteroids in the form of intravenous pulse therapy are used to treat autoimmune disorders like pemphigus[1],bullous pemphigoid, vitiligo, alopecia areata[2].Oral steroid minipulse has been tried in conditions like vitiligo[3],alopecia areata[4,5].Corticosteroids steroids like betemethasone[4],prednisolone[5] and methylprednisolone[3] has been used for minipulse therapy .Oral methylprednisolone has been used safely in pediatric age group[3] also. The side effects of steroids are minimal when given in the form of pulse therapy compared to daily conventional dose.

Hyperglycemia is one of the many known side effects of corticosteroid therapy, particularly when these drugs are administered in high doses[6].The pattern of steroid induced hyperglycemia is post-prandial hyperglycemia[7].

Acute hyperglycemia and ongoing high blood glucose levels have been linked to increased risk for infection, poor cardiovascular outcome, thrombosis, inflammation, endothelial cell dysfunction and enhanced neuronal damage after ischaemic brain injury[6].

One of our patient who was on oral methylprednisolone minipulse met with a road traffic accident .after hospitalization it was found that his blood sugar was more than 450mg/dl .He required emergency measures to bring down the blood sugar

levels. We initiated this study to know the effects of oral methylprednisolone minipulse on blood sugar.

Aim & Objective

AIMS AND OBJECTIVES

1. To determine post-prandial blood sugar before and after giving oral methylprednisolone minipulse.
2. To observe for hyperglycemic symptoms.

Review of Literature

STEROIDS

History

Addision described fatal outcomes in patients with adrenal destruction in a presentation to the South London Medical Society in 1849. These studies were soon extended when Brown – Sequard demonstrated that bilateral adrenalectomy was fatal in laboratory animals. It later was shown that the adrenal coetex, rather than the medulla, was essential for survival in these experiments.

Studies of the factors that regulated carbohydrate metabolism (termed glucocorticoids) culminated with the synthesis of cortisone, the first pharmacologically effective glucocorticoid to become readily available. Subsequently, Tate and colleagues isolated and characterized a distinct corticosteroids, aldosterone, which potently affected fluid and electrolyte balance and therefore was termed a mineralocorticoid. The isolation of distinct corticosteriods that regulate carbohydrate metabolism or fluid and electrolyte balance led to the concept that the adrenal cortex comprises two largely independent units: an outer zone that produces mineralcorticoids and an inner region that synthesizes glucocorticoids and androgen precursors.

Studies of adrenocortical steroids also played a key part in delineating the role of the anterior pituitary in endocrine function. As early as 1912, Cushing described patients with hypercorticism, and later recognized that pituitary basophilism caused the adrenal over activity, thus establishing the link between the anterior pituitary and adrenal function. These studies led to the purification of ACTH and the determination of its chemical structure. ACTH was further shown to be essential for maintaining the

structural integrity and steroidogenic capacity of the inner cortical zones. Harris established the role of the hypothalamus in pituitary control and postulated that a soluble factor produced by the hypothalamus activated ACTH release. These investigations culminated with the determination of the structure of corticotrophin releasing hormone (CRH), a hypothalamic peptide that regulate secretion of ACTH from the pituitary.

Action on the Adrenal Cortex

Acting via MC2R, ACTH stimulates the adrenal cortex to secrete glucocorticoids, mineralocorticoids, and the androgen precursor dehydroepiandrosterone (DHEA) that can be converted peripherally into more potent androgens. The adrenal cortex histologically and functionally can be separated into three zones that produce different steroids products under different regulatory influences. The outer Zona glomerulosa secretes the glucocorticoid cortisol, and the inner zona reticularis secretes DHEA and its sulfated derivative.

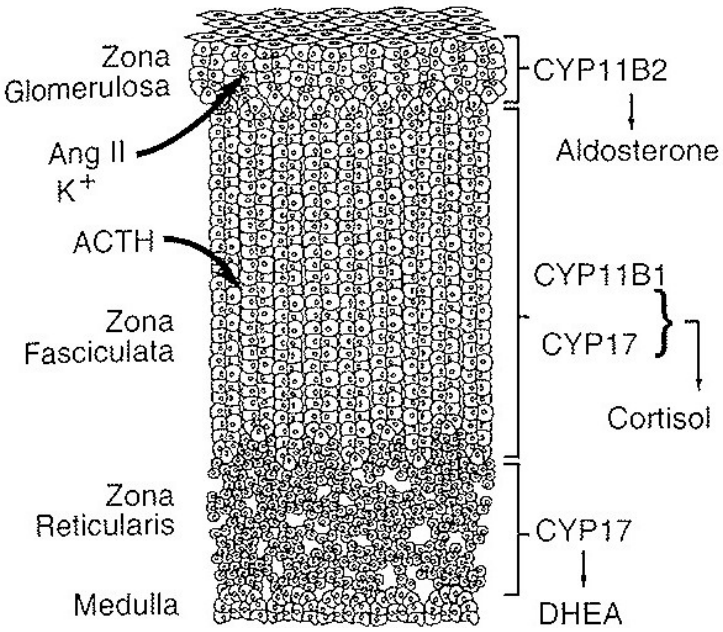

Fig: The adrenal cortex contains three anatomically and functionally distinct compartments.

Cells of the outer zone have receptors for angiotensin II and express aldosterone synthase (CYP11B2), an enzyme that catalyzes the terminal reactions in mineralocorticoid biosynthesis. Although ACTH actuetly stimulates mineralocorticoid production by the zona glomerulosa, this zone is regulated predominantly by angiotensin II and extracellular K+ and does not undergo atrophy in the absence of ongoing stimulation by the pituitary gland. In the setting of persistently elevated ACTH, mineralocorticoid levels initially increase and then return to normal.

In contrast, cells of the zona fasciculata have fewer receptors for angiotensin II and express two enzymes, steroid 17 α-hydroxylase (CYP17) and 11β-hydroxylase (CYPIIB1), which catalyze the production of glucocorticoids. In the zona reticularis, CYP17 carries out a second 17-20 lyase reaction that converts C21 corticosteroids to C 19 androgen precursors.

In the absence on the anterior pituitary, the inner zones of the cortex atrophy, and the production of glucocorticoids and adrenal androgens is markedly impaired.Persistently elevated levels of ACTH, due either to repeated administration of large doses of ACTH or to excessive endogenous production, induce hyperplasia and hypertrophy of the inner zones of the adrenal cortex, with overproduction of cortisol and adrenal androgens. Adrenal hyperplasia is most marked in congenital disorders of steroidogenesis, in which ACTH levels are continuously elevated as a secondary response to impaired cotrisol bio synthesis. There is some debate regarding the relative roles of ACTH versus other POMC derived peptides in stimulating adrenal growth, but the essential role of the anterior pituitary in maintaining the integrity of the zone fasciculata is indisputable.

Hypothalamic – Pituitary – Adrenal Axis

The rate of glucocorticoid secretion is determined by fluctuations in the release of ACTH by the pituitary corticotropes. These corticotropes, in turn, are regulated by corticotrophin-releasing hormone (CRH), a peptide hormone released by CRH neurons of the endocrine hypothalamus. These three organs collectively are referred to as the hypothalamic- pituitary- adrenal (HPA) axis, an integrated system that maintains appropriate levels of glucocorticoids. There are three characteristic modes of regulation of the HPA axis: diurnal rhythm in basal steroidogenesis, negative feedback regulation by adrenal corticosteroids, and marked increase in steroidogenesis in response to stress. The diurnal rhythm is entrained by higher neuronal centers in response to sleep- wake cycles, such that levels of ACTH peak in the early morning hours, causing the circulating glucocorticoid levels to peak at approximately 8 A.M. As discussed below, negative feedback regulation occurs at

multiple levels of the HPA axis and is the major mechanism that maintains circulating glucocorticoid levels in the appropriate range. Stress can override the normal negative feedback control mechanisms, leading to marked increase in plasma concentrations of glucocorticoid.

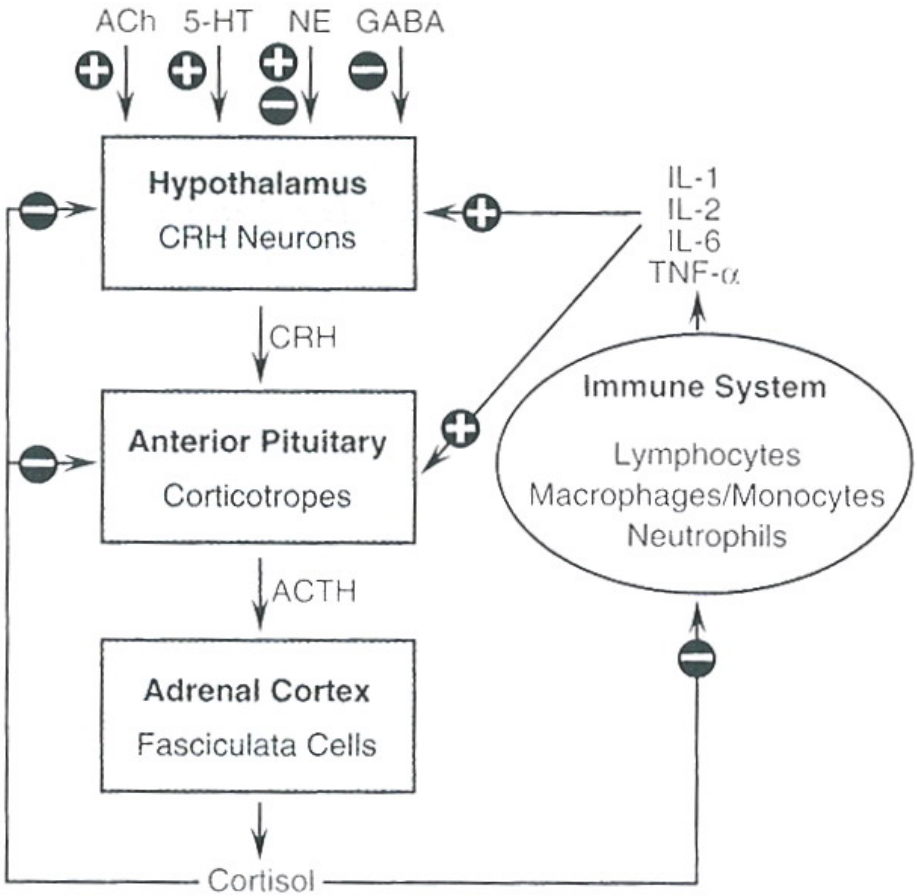

Fig: Overview of the hypothalamic-pituitary-adrenal (HPA) axis and the immune inflammatory network.

Negative Feedback of Glucocorticoids

Glucocorticoids inhibit ACTH secretion via direct and indirect actions on CRH neurons to decrease CRH mRNA levels and CRH release and via direct effects on corticotropes. The inhibition of CRH release may be mediated by specific

corticosteroid receptors in the hippocampus. At lower cortisol levels, the mineralcorticoid receptor (MR), which has a higher affinity for glucocorticoids and is the predominant form found in the hippocampus, is the major receptor species occupied. As glucocorticoid concentrations rise and exceed the capacity of the MR, the glucocorticoid receptor (GR) also becomes occupied. Both classes of receptor apparently control the basal activity of the HPA axis, whereas feedback inhibition by glucocorticoids predominantly involves the GR.

The Stress Response

Stress overcomes negative feedback regulation of the HPA axis, leading to a marked rise in corticosteroid production. Example of stress signals include injury, hemorrhage, severe infection, major surgery, hypoglycemia, cold, pain and fear. Although the precise mechanisms that underlie this stress response and the essential actions played by corticosteroids are not fully defined, it is clear that their increased secretion is vital to maintain homeostasis in these stressful settings. As discussed below, complex interactions between the HPA axis and the immune system may be a fundamental physiological component of this stress response.

Adrenocortical steroids

The adrenal cortex synthesizes two classes of steroids, the corticosteroids (glucocorticoids and mineralocorticoids) and the androgens. The actions of corticosteroids historically were described as glucocorticoid (carbohydrate metabolism - regulating) and mineralocorticoid (electrolyte balance - regulating). In humans cortisol (hydrocortisone) is the main glucocorticoid and aldosterone is the main mineralocorticoid.

Pharmacology

Structure

The basic structure of all corticosteroids consists of three hexane rings and one pentane ring[8]. The ring structure is known as the cyclopentano perhydrophenanthrene nucleus. Cortisone and hydrocortisone both possess a 4, 5 double bond and a ketone carbonyl group at the 3 position 2,3. Cortisone which is an inactive form has a ketone at the 11 position. The active from, hydrocortisone (cortisol) is formed through hepatic conversion of the 11- ketone to an 11-hydroxyl group. Prednisone is formed by addition of a 1, 2 double bond and through 11-hydroxylation the active analog prednisolone is formed. By the addition of a 6 – methyl group to prednisolone,. methyl prednisolone is formed.

Absorption and transport

Corticosteroids provided exogenously are absorbed in the upper jejunum . Food delays, but does not decrease the amount of prednisone absorbed. Peak plasma levels are reached 30-100 minutes after drug is taken.

After absorption 90% or more of cortisol in plasma is reversibly bound to protein under normal circumstances .Only the unbound corticosteroid can enter cells to mediate corticosteroid effects. Two plasma proteins account for steroid binding capacity: corticosteroid binding protein (CBG; also called transcortin) and albumin. CBG is the primary endogenous carrier protein[8].

CBG is decreased by hypothyroidism, liver disease, renal disease, and obesity all of which result in increased amount of corticosteroid free fraction[10]. CBG is

increased by estrogen therapy, pregnancy and hyperthyroidism, all decrease the corticosteroid free fraction .All endogenous and synthetic corticosteroids are well distributed into fetal tissue with the exception of prednisone[8].

Compound	**Anti inflammatory potency**	**Na^+ - Retaining Potency**	**Duration of action***	**Equivalent dose, MG**
Cortisol	1	1	S	20
Cortisone	0.8	0.8	S	25
Fludrocortisone	10	125	I	-
Prednisone	4	0.8	I	5
Prednisolone	4	0.8	I	5
6α - Methylprednisolone	5	0.5	I	4
Triamcinolone	5	0	I	4
Betamethasone	25	0	L	0.75
Dexamethasone	25	0	L	0.75

S - Short (8-12 hour biological half –life)

I – Intermediate (12-36 hour biological half –life)

L – Long (36 - 72 hour biological half –life)

Metabolism and excretion

The adrenocortical steroids have a double bond in the 4, 5 – position and a ketone group at C3. Reduction of 4, 5 double bond occurs at both hepatic and extrahepatic sites yielding inactive compounds. Subsequent reduction of the 3- ketone

substituent to the 3 – hydroxyl derivative forming tetrahydrocortisol, occurs only in the liver. These A-ring reduced steroids are conjugated in the liver forming sulfate esters and glucuronides which are water soluble and excreted in urine.

Mechanisms for corticosteroid effects

Corticosteroids interact with specific receptor proteins in target tissues to regulate the expression of corticosteroid responsive genes, thereby changing the levels and array of proteins synthesized by the various target tissues. (Fig) As a consequence of the time required to modulate gene expression and protein synthesis, most effects of corticosteroids are not immediate but become apparent after several hours.

Although corticosteroids predominantly act to increase expression of target genes, there are well documented examples in which corticosteroids decrease transcription of target genes. In addition to these genomic effects some immediate actions of corticosteroids may be mediated by membrane a bound receptors

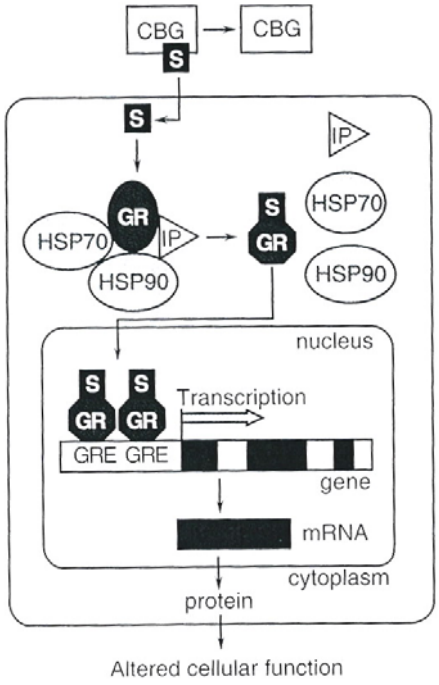

Fig: Intracellular mechanism of action of the glucocorticoid receptors

Glucocorticoid Receptors

The Glucocorticoid receptor resides predominantly in the cytoplasm in an inactive form until it binds glucocorticoids .Steroid binding results in receptor activation and translocation to the nucleus. The inactive GR is complexed with other proteins, including Heat shock protein 90; HSP 70 and a 56,000 dalton immunophilin, one of the group of intracellular proteins that bind the immunosuppressive agents cyclosporine and tacrolimus. HSP 90, through interactions with the steroid-binding domain may facilitate folding of the GR into an appropriate conformation that permits ligand binding.

The GR are members of the nuclear receptor family of transcription factors that transduce the effects of a diverse array of small, hydrophobic ligands, including

the steroid hormones, thyroid hormones, vitamins D and retinoids. Mutations leading to partial loss of glucocorticoid receptor function have been identified in rare patients with generalized glucocorticoid resistance .

Regulation of Gene Expression by corticosteroids

After ligand binding, the GR dissociates from its associated proteins and translocates to the nucleus. In the nucleus it interacts with specific DNA sequences within the regulatory regions of affected genes. The short DNA sequences that are recognized by the activated GR are called glucocorticoid responsive elements. It provides specificity to the induction of gene transcription by glucocorticoids.

The mechanism by which GR activates transcription are complex and not completely understood, but they involve the interaction of the GR with transcriptional coactivators and with proteins that make up the basal transcription apparatus. The recognition that the metabolic effects of glucocorticoids generally are mediated by transcription, while the anti-inflammatory effects are mediated by transrepression, suggests that selective GR ligands may maintain the anti-inflammatory actions while lessening the metabolic side effect.

The GR and MR differ in their ability to inhibit AP -1 mediated gene activation, suggesting that differential interactions with other transcription factors may underlie their distinct effects on cell function. In addition the MR has a restricted effects on cell function. MR is expressed mainly in the kidney (distal convoluted tubule and collecting duct), colon, salivary glands, sweat glands and hippocampus.

Receptor-Independent Mechanism for corticosteroid specificity

The type 2 isozyme of 11β – hydroxysteroid dehydrogenase (11βHSD_2) plays a key role in corticosteroid specificity, particularly in the kidney, colon and salivary glands. This enzyme metabolizes glucocorticoids such as cortisol to receptor-inactive 11-keto derivatives such as cortisone. Because its predominant form in physiological settings is the hemiacetal derivative, which is resistant to 11 βHSD action, aldosterone escapes this reactivation and maintains mineralocorticoid activity. In the absence of 11 βHSD2, as occurs in an inherited disease called the syndrome of apparent mineralocorticoid excess, the MR is swamped by cortisol, leading to severe hypokalemia and mineralocorticoid – related hypertension. A state of mineralocorticoid excess also can be induced by inhibiting 11 βHSD with glycyrrhizic acid, a component of licorice implicated in licorice – induced hypertension.

Physiological Functions

The effect of corticosteroids include alterations in carbohydrate, protein, and lipid metabolism; maintenance of fluid and electrolyte balance; and preservation of normal function of cardiovascular system, the immune system, the kidney, skeletal muscle, the endocrine system, and the nervous system. In the absence of adrenal cortex, survival is made possible only by maintaining an optimal environment, including adequate and regular feedings, ingestion of relatively large quantity of sodium chloride, and maintenance of an appropriate environmental temperature, stresses such as infection and trauma in this sitting can be life threatening. The anti-inflammatory and immunosuppressive actions of corticosteroids – one of the major "pharmacological" uses of this class of drugs – also provide a protective mechanism in the physiological setting.

Corticosteroids are grouped according to their relative potencies in Na+ retention, effects on carbohydrate metabolism (ie. Hepatic deposition of glycogen and gluconeogenesis and anti-inflammatory effects). The corticosteroids traditionally are divided into mineralocorticoids and glucocorticoids.

Carbohydrate and protein metabolism

Corticosteroids stimulate the liver to form glucose from amino acids and glycerol and to store glucose as liver glycogen. In the periphery glucocorticoids diminish glucose utilization, increase protein breakdown and the synthesis of glutamine, and activate lipolysis, thereby providing amino acids and glycerol for gluconeogenesis. The net result is to increase blood glucose levels. Because of their effects on glucose metabolism glucocorticoids can worsen glycemic control in patients with overt diabetes and can precipitate the onset of hyperglycemia in patients who are otherwise predisposed.

Lipid metabolism

Two effects of corticosteroids on lipid metabolism. First is the dramatic redistribution of body fat that occurs in settings of endogenous or pharmacologically induced hypercorticism, such as Cushing's syndrome. The other is the permissive facilitation of the lipolytic effect of other agents such as growth hormone and β adrenergic receptor agonists, resulting in an increase in free fatty acids after glucocorticoid administration. With respect to fat distribution, there is increased fat in the back of the neck ("buffalo hump") face ("moon facies") and supraclavicular area, coupled with a loss of fat in the extremities.

Electrolyte and water balance

Aldosterone is by far the most potent endogenous corticosteroid with respect to fluid and electrolyte balance. Thus electrolyte balance is relatively normal in patients with adrenal insufficiency due to pituitary disease. Mineralocorticoids act on the distal tubules and collecting ducts of the kidney to enhance reabsorption of Na^+ from the tubular fluid; they also increase the urinary excretion of K+ and H+. The primary features of hyperaldosteronism are Na+ balance with consequent expansion of extracellular fluid volume, normal or slight increase in plasma Na+ concentration,hypokalemia and alkalosis.Mineralocorticoid deficiency leads to Na+ wasting and contraction of the extracellular fluid volume, hyponatremia, hyperkalemia and acidosis. Glucocorticoids play a permissive role in the renal excretion of free water.

Glucocorticoids also exert multiple effects on $Ca2^+$ metabolism. Steroids interfere with $Ca2^+$ uptake in the gut and increase $Ca2^+$ excretion by the kidney. These effects collectively lead to decreased total $Ca2^+$ stores.

Cardiovasular system

The effects of corticosteroids on the cardiovascular system result from mineralocorticoid – induced changes in renal Na+ excretion, as is evident in primary aldosteronism. The resultant hypertension can lead to a diverse group of adverse effects on the cardiovascular system, including increased atherosclerosis, cerebral hemorrhage, stroke and hypertensive cardiomyopathy.

The second major action of corticosteroids on the cardiovascular system is to enhance vascular reactivity to other vasoactive substances. Hypoadrenalism is

associated with reduced response to vasoconstrictors such as nor- epinephrine and antiotensin II, perhaps due to decreased expression of adrenergic receptors in the vascular wall.

Skeletal muscle

Corticosteroids are required for the normal function of skeletal muscle, and diminished work capacity is a prominent sign of adrenocortical insufficiency. In patients with addison's disease, weakness and fatigue are frequent symptoms that may reflect on inadequacy of the circulatory system.

In primary aldosteronism, muscle weakness results primarily from hypokalemia rather than from direct effects of mineralocorticoids on skeletal muscle. In contrast glucocorticoid excess over prolonged periods either secondary to glucocorticoid therapy or endogenous hypercortism, causes skeletal muscle wasting. This effect termed steroid myopathy, accounts for weakness and fatigue in patients with glucocorticoid excess.

Formed elements of blood

Glucocorticoids exert minor effects on hemoglobin and erythrocyte content of blood as evidenced by the frequent occurance of polycythemia in cushings syndrome and of normochromic normocytic anemia in adrenal insufficiency. More profound effects are seen in the setting of autoimmune hemolytic anemia, in which the immunosuppressive effects of glucocorticoids can diminish the self – destruction of erythrocytes.

Addisons disease is associated with an increased mass of lymphoid tissue and lymphocytosis. Cushing's syndrome is characterized by lymphocytopenia and decreased mass of lymphoid tissue.

Central nervous system

Corticosteroids exert a number of indirect effects on the CNS, through maintenance of blood pressure, plasma glucose concentrations and electrolyte concentrations .Increasingly, direct effects of corticosteroids on the CNS have been recognized, including effects on mood, behavior and brain excitability.

Anti-inflammatory and Immunosuppressive actions

Glucocorticoids can prevent or suppress inflammation in response to multiple inciting events, including radiant, mechanical, chemical, infectious and immunological stimuli.

Clinical Uses:

Pemphigus vulgaris:

Systemic corticosteroids remain the mainstay of treatment of pemphigus. The emphasis here is high dose corticosteroid therapy with use of adjunctive steroid – sparing "immunosuppressive therapy. Adjunctive therapy is generally used with a choice of Azathioprine, cyclophosphamide, cyclosporine, methotrexate, gold or plaspmapheresis. [11, 12, 13] Pulse methylprednisolone may be indicated to attain rapid disease control in more severe cases of pemphigus vulgaris[14]. Pulse dexamethasone and cyclophosphamide have been documented as an effective option for moderate to severe pemphigus vulgaris[15]. Early reports on oral corticosteroid therapy for

pemphigus vulgaris describe doses of 120-140 mg daily of prednisone[15, 16]. For mild to moderate disease the starting dose of prednisolone is 60- 80 mg/day, whereas for severe disease treatment is started with 80-120 mg/day[17].

Bullous pemphigoid

In Bullous pemphigold patients, moderate doses of corticosteroid upto 1mg/kg daily are used [12]. The suggested initial doses are 20mg or 0.3mg/kg body weight daily in localized or mild disease, 40mg or 0.6mg/kg per day in moderately severe disease and 50-70mg or 0.75 mg/kg daily in severe disease. About half of the patients require concomitant immunosuppressive therapy with drugs such as azathioprine or methotrexate[19, 20]. Deaths still occasionally occur in older patients with more extensive involvement; more conservative management utilizing alternatives to corticosteroid may help in decreasing the risk of sepsis.

Cicatricial pemphigoid

Cicatricial pemphigoid is less responsive to corticosteroid that in bullous pemphigoid [18, 22]. But still it remains the mainstay initial drugs for moderate-to-severe cicatricial pemphigoid [28]. In general 1 – 15mg/kg daily of prednisolone is required for initial control of moderate – to severe cases.Once the disease is controlled, prednisolone should be slowly tapered while continuing with immunosuppressive. Dapsone (50 – 200mg/d) is another initial treatment option and if satisfactory results are not achieved in 3 months treatment with prednisolone and cyclophosphamide should be started[24].

Vitligo

The most frequently used modalities in the treatment of vltiligo are PUVA and topical corticosteroids[25]. In actively spreading vitiligo, PUVA therapy in not an ideal treatment. There have been a few reports on the use of systemic steroids in vitiligo therapy. Indian dermatologist, Desai and others have long believed that systemic prednisolone is a helpful adjunct to photoyherapy.Therapy with betamethasone was reported by Pasricha and Khaitan to minimize its side effects[27]. Another oral mini – pulse therapy was studied by Kanwar et al in 37 patients with rapidly spreading vitiligo they received dexamethasone minipulse[28].

Alopecia areata

Despite protestations that systemic steroids have no place in the therapeutic plan for alopecia areata, they continue to be used by "Pragmatists." Most authorities agree that systemic steroid therapy has a place in arresting the spread of rapidly progressing alopecia areata threatening to become total[29]. Systemic steroids have been used in various regimens and dosages in the treatment of extensive alopecia areata with variable responses. The high doses of intravenous methylprednisolone for 3 days per month have shown good results in patients with multifocal alopecia areata and alopecia totalis. In another study by Doulat Rai Bajaj and et.al showed that prednisolone oral minipulase therapy is a convenient and effective therapy for the treatment of extensive alopecia areata[30].

Steven Johnson Syndrome and Toxic epidermal Necrolysis

A number of studies support routine Corticosteroid therapy [31, 32] .But still there is controversy regarding the use of systemic corticosteroid for the spectrum of Steven Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). Experience of routine systemic corticosteroid use suggest that for SJS and TEN patients, systemic corticosteroid treatment early in the disease process (before significant sloughing of skin), followed by rapid tapering of corticosteroid may be beneficial and even life saving[33]. Intravenous methylprednisolone in divided doses upto 2 – 2.5 mg/kg daily is indicated initially, with relatively rapid tapering when new blister formation ceases.

Erythema multiforme minor

A Common indication for moderate corticosteroid doses is recurrent oral erythema multiforme (EM) minor. Painful oral erosions respond promptly to prednisolone of doses upto 1mg/kg daily, rapidly tapered over 2 – 3 weeks.

Lupus erythematosus spectrum

Corticosteroid therapy is generally indicated for systemic disease manifestations of lupus erythematosus spectrum. Primary cutaneous indications are LE patients with vasculitis and bullous lupus erythematosus, widespread disfiguring discoid lupus erythematosus[34]. Numerous alternatives like anti malarial agents, dapsone, retinoids, thalidomide and oral gold are available. And moreover most cutaneous LE cases can be managed with sunscreens, topical or intralesional CS and antimalarial therapy. Doses of 20 mg every day upto 60mg daily of prednisolone may be required.

Dermatomyositis

Corticosteroids are the first line agents[36]. Corticosteroids often as monotherapy is indicated in Dermatomyositis. Dermatomyositis is a condition in which very slow tapering of syetemic oral corticosteroids over atleast 3-6 months is needed. About 90% of patients respond to a prednisolone of dose 1-1.5 mg/kg daily. The dose is adjusted on the basis of muscle strength and muscle enzyme levels.

Vasculitis

Vasculitis is the cutaneous manifestations of a variety of conditions. The most common presentations are palpable purpura from leukocytoclastic vasculitis and persistant urticaria lesions associated with urticarial vasulitis. Gastrointestinal, renal and joint involvement may indicate systemic corticosteroid therapy. [37, 38] Doses of upto 1 mg/kg/d of prednisolone is used successfully for patients with chronic cutaneous leukocytoclastic vasculitis with ulcers, infarction or persistent painful lesions. And rapid tapering to alternate –day dosing is suggested, prednisolone 20 mg (or less) on alternate days is often used. Colchine is an effective alternative to corticosteroid therapy in most cases of chronic cutaneous leukocytoclastic vasculitis.

Pyoderma Gangrenosum

Systemic corticosteroids are considered as the drug of choice for the treatment of pyoderma gangrenosum and are particularly effective in treating the acute, rapidly progressive form of the disease. Initial doses of prednisolone in the range of 40 – 80mg/day of higher are usually required. In some cases steroid pulse therapy may produce rapid improvement of the disease that was unresponsive or oral corticosteroids; methylprednisolone or dexamethasone pulse therapy has produced

good results[39]. Intralesional corticosteroid may be a useful adjunct to the above two systemic therapies.

Lichen Planus

Systemic steroids are helpful in treating generalized eruptive lichen planus, erosive (ulcerative) oral and genital lichen planus, progressive lichen planus and the active stage of scalp lichen planus causing alopecia. Prednisolone given at 40 – 60 mg daily and tapered overy 4-6 weeks consistently eradicates or reduces the intensity of generalized lichen planus. Ideally the regimen should reach a physiologic dose range by 3 – 4 weeks. This corticosteroid use is potentially important for darkly pigmented races in whom pigment incontinence is most notable. Alternatives such as high potency topical corticosteroid gels, intralesional corticosteroid therapy, systemic retinoids and cyclosporine all should be considered for patients with oral lichen planus.

Acute dermatitis

Severe acute contact dermatitis due to poison ivy/poison oak is a classic situation in which 2 to 3 week burst of systemic corticosteroid therapy is usually successful at minimal risk to the patient. Doses upto 1 mg/kg/day tapered over 2 – 3 weeks yields adequate improvement with minimal risk of rebound flare after cessation of therapy. Doses of prednisolone less than 1mg/kg/day is commonly used for acute flares of chronic dermatitis. Exfoliative dermatitis commonly requires systemic steroids. Excluding psoriasis exfoliative erythroderma refractory to aggressive topical medication or to phototherapy may respond to prednisolone upto 1mg/kg/day. This dose is tapered rapidly to low dose alternate day therapy.

Sarcoidosis

Ulcerative sarcoidosis or aggressive facial involvement like in lupus pernio may indicate systemic corticosteroid therapy. Alterations include antimalarial agents, low dose methotrexate and intralesional corticosteroids.

Androgen excess syndromes

For recalcitrant acne vulgaris and hirsutism due to elevated adrenal androgens, corticosteroid therapy is often indicated. Night time suppressive therapy with low dose dexamethasone 0.125 – 0.375mg.[45] This timing is important to suppress the early morning peak of ACTH, which stimulates adrenal androgen production.

Post – Herpetic Neuralgia

A study by Eaglstein suggested that moderate –dose corticosteroid could minimize the risk of post herpetic neuralgia. It is reasonable to treat patients with facial involvement, patients with severe acute pain during the cutaneous eruption and patients over 55-60 years of age with combined antiviral and corticosteroid therapy. It is suggested recently that the systemic corticosteroid have a greater role in treating acute pain of herpes zoster than for preventing post – herpetic neuralgia.

Contraindication

Absolute

Systemic fungal infections

Herpes simples keratitis

Hypersensitivity (with ACTH, IV preparations)

Relative

- Cardiovascular
  - Hypertension
  - Congestive heart failure
- Central nervous system
  - Prior psychosis
  - Severe depression
- Infections
  - Active TB
  - Positive tuberculin test
- Metabolic
  - Diabetes mellitus
- Musculoskeletal
  - Osteoporosis
- Ocular
  - Cataracts
  - Glaucoma
- Pregnancy

Adverse effects of steroids

HPA axis

- Steroid withdrawl syndrome
- Addisonian crisis.

Glucocorticoid effects

Hyperglycemia

Increased appetite (and weight)

Mineralocorticoid effects (due to sodium retention, potassium loss)

Hypertension

Congestive heart failure

Excessive weight gain

Hypolcalcemia

Lipid effects (↑ lipolysis and altered deposition)

Hypertriglyceridemia

Cushingoid changes

Menstrual irregularity

Bone and related metabolic effects

Osteoporosis

Osteonecrosis

Hypocalcemia

Gastrointestinal

Peptic ulcer disease

Bowel perforation

Fatty liver changes

Esophageal reflux

Nausea, vomiting

Ocular effects

Cataracts

Glaucoma

Infections

Refraction Changes

Psychatric

Psychosis

Agitation or personality change

Depression

Prednisolone phobia or dependency

Neurologic

Pseudotumor cerebri

Epidural lipomatosis

Peripheral neuropathy

Infectious

Tuberculosis reactivation

Opportunistic – Deep fungi, others

Prolonged herpes virus infections.

Muscular

Myopathy

Pediatric

Growth impairment

Pulse IV therapy

Electrolyte shifts

Cardiac dysrrythmias

Seizures

Potentially fatal complications

Adrenal crisis (Addisonian crisis)

Such patients exhibit characteristic symptoms of adrenal insufficiency, hypotension and markedly decreased cortisol levels. In the current era this complication is extraordinarily rare.

Bowel perforation

Tremendous caution should be given with the use of systemic corticosteroids after recent bowel anastomosis and for patients with active dliverticulitis.

Peptic ulcer perforation

This is more likely with adjunctive non-steroidal anti – inflammatory drugs and in patients with a prior peptic ulcer disease.

Pancreatitis

This complication largely occurs with triglycerides>800 mg/dl severe hyperglycemia (Diabetic ketoacidosis or hyperosmolar non-ketotic coma).

Most severe hyperglycemia occurs with pre existing diabetes mellitus, the widespread availability to home glucose monitoring should make this a rare complication.

Opportunistic infections

These infections are uncommon with corticosteroids used for dematologic indications and it primarily occurs with multidrug immunosuppression regimens for systemic autoimmune disorders and for organ transplantation.

Immunosuppresion carcinogenesis

Opportunistic malignancies denote kaposi's sarcoma, non-hodgkins lymphoma, squamous cell carcinoma that are common in organ transplantation patients. This is very uncommon with systemic corticosteroids for purely dermatologic indications.

Other Adverse effects

Osteonecrosis (Avascular necrosis, aseptic necrosis):

The majority of osteonecrosis cases are with pharmacologic doses of prednisone (or comparable doses of other systemic corticosteroids) for at least 2 – 3 months for life threatening conditions.

Osteoporosis

Preventive measures to retard the expected corticosteroid induced bone calcium depletion for any patient receiving pharmacologic doses of corticosteroid for atleast one month are imperative. The options includes calcium (1000 – 1500 mg daily), vitamin D (800 U daily), bisphosphonates, estrogens, and calcitonin.

Growth impairment in Children

This is rare with dermatological indications.

Cutaneous adverse effects from systemic corticosteroids

Wound healing and related changes

- Non healing wounds, ulcers, striae, atrophy, telangiectasis,

Pilosebaceous

Steroid ance, steroid rosacea,

Vascular

Purpura, including actinic purpura

Cutaneous infections

Staphylococal, herpes virus infections

Hair effects

Telogen effluvium, hirsutism

Injectable corticosteroid

Fat atrophy, crystallization of injectable material

Other skin effects

Pustular psoriasis is rare, rebound of poison ivy /oak, acanthosis nigricans

STEROID INDUCED HYPERGLYCEMIA

Hyperglycemia is one of the many known side effects of corticosteroid therapy, particularly when these drugs are administered in high doses [41,42] Corticosteroids stimulate the liver to form glucose from amino acids and to store glucose as liver glycogen. In the periphery glucocorticoids diminish glucose utilization, increase protein breakdown and the synthesis of glutamine, and activate lipolysis, thereby providing amino acids and glycerol for gluconeogenesis. The net result is to increase blood glucose levels. Because of their effects on glucose metabolism, glucocorticoids can worse glycemic control in patients with overt diabetes and can precipitate the onset of hyperglycemia, in patients who are otherwise predisposed.

The mechanism by which glucorticoids inhibit glucose utilization in peripheral tissues are not fully understood. Glucocorticoids decrease glucose uptake in adipose tissue, skin, fibroblasts, thymocytes and polymorphonuclear leukocytes, these effects are postulated to result from translocation of the glucose uptake in adipose tissue, effects are postulated to result from translocation of the glucose transporters from the plasma membrane to an intracellular location. These peripheral effects are associated with a number of catabolic actions, including atrophy of lymphoid tissue, decreased muscle mass, negative nitrogen balance and thinning of the skin.

Similarly the mechanisms by which the glucocorticoids promote gluconeogenesis are not fully defined, Amino acids mobilized from a number of tissues in response to glucocorticoids reach the liver and provide substrate for the production of glucose and glycogen, In the liver glucocorticoids induce the transcription of a number of enzymes involved in gluconeogenesis and amino acid

metabolism including phosphoenol pyruvate corboxykinase (PEPCK), glucose 6-phosphatase and the bi-functional enzyme fructose – 2, 6 – bisphosphatase. Analyses of the molecular basis for regulation of PEPCK gene expression have identified complex regulatory influences involving an interplay among glucocorticoids, insulin, glucagon and catecholamines.The effect of these harmones and amines on PEPCK gene expression mirror the complex regulation of gluconeogenesis in the intact organism.

St. Louis, July 17, 2003 found that a protein called peroxisome proliferator – activated receptor alpha (PPAR - alpha) is critical in this process and liver plays a role. PPAR – alpha is found in the liver, kidney, muscles, blood vessels and other organs, since it is activated by fatty acids and since glucocorticoids alter fatty acid processing, Bernal –Mizra-Chi and his colleagues hypothesized that the two may act together to produce the disease –causing side effects[48]. They therefore compared mice lacking both LDLR and PPAR- alpha with mice lacking only LDLR (receptor for low density lipoprotein also known as "bad cholesterol").

They found that when given the glucocorticoid dexamethasone, mice lacking only LDLR had increased levels of insulin, fasting glucose and leptin, all signs of diabetes. Mice lacking both LDLR and PPAR – alpha shoved no sings of diabetes.

In a recent position statement, the American Diabetes association identified corticosteroids as agents that contribute to the occurrence of hyperglycemia[44].

Hyperglycemia was defined as a blood glucose level ≥200 mg/dl from either a bedside or a laboratory glucose measurement.

An excess of steroids impairs the suppression of glucose production and stimulation of glucose utilization, which might cause diabetes mellitus or aggravate preexistent diabetes. According to these mechanisms abnormal glucose metabolism induced by steroids may reflect both fasting and post-prandial hyperglycemia. The diabetes epidemiology; collaborative analysis of diagnostic criteria in asia study in Japan demonstrated that more than 70% if diabetes mellitus cases were diagnosed based on post-prandial hyperglycemia. In a study done by Greenstone and Shaw[45] measuring blood glucose level normalized throughout the next day. Hyperglycemia induced by glucocorticoids is primarily an exaggeration of post prandial hyperglycemia. Most patients will not have significantly different fasting blood glucose levels when they are receiving corticosteroids. Glucocorticoids increase hepatic glucose production and can inhibit insulin – stimulated glucose uptake in peripheral tissues.[46]

Also in a study conducted among the patients with primary renal diseases all of the 17 patients were diagnosed as having diabetes mellitus by postprandial hyperglycemia with normal fasting blood glucose levels.[47]

In another study conducted in 102 patients with rheumatoid arthritis treated with methyl prednisolone 8.8% of patients developed diabetes mellitus and six patients with existing diabetes mellitus in whom glycaemic control worsened between three to six months.[48]

In yet another study with high dosage treatment of methylprednisolone therapy in severe acute respiratory syndrome of one hundred of thirty three cases. 36.3% were diagnosed as corticosteroid induced diabetes[49]. These patients were treated with high doses of methylprednisolone had increased blood sugar level when compared with

patients treated with corticosteroids of low doses. If the patients were treated with an average dose less than 90 mg/day and treatment duration shorter than 15 days the diabetes incidence was 10.5%.

In a literature review, they showed that the total glucocorticoid dose and duration of therapy are strong predictors of diabetes induction other risk factors include age and body mass index[50]. Failure to treat glucocorticoid induced hyperglycemia is related to the presumed short duration of administration of glucocorticoid treatment and the emphasis of fasting plasma glucose only.

Fluctuations in plasma glucose concentrations, however has been associated with increased cardiovascular mortality[51]. A mechanism for this relationship is suggested by studies showing that even short-term or postprandial hyperglycemia is associated with acute inflammation and endothelial dysfunction in patients without diabetes and in those with type 2 diabetes mellitus.[52] Moreover reduced fluctuation in glucose levels with administration of insulin decreases these defects.[53]

Virtually all currently available agents used in the treatment of type 2 diabetes mellitus have been suggested as treatment options for glucocorticoid induced hyperglycemia.[54] These include sulphonylureas, metformin, thiazolidinediones (TZDS) and insulin .Each agent has inherent limitations in patients who require Glucocorticoids.[55] Long acting sulphonylureas were first used in the long term treatment of renal transplant patients, with response rates of 25%. The agents have been used in non transplant patients as well. The advantages of these agents are their prompt insulin secretory effect and their low cost. Prolonged duration of action with most of the agents may increase the risk of hypoglycemia when short term and tapering doses of glucocorticoids are prescribed. Shorter acting agents such as

repaglinide or nateglinide might be more suitable metformin would seem to be a reasonable agent because of its effect on insulin sensitivity. In patients requiring long term glucocorticoid use in whom renal and liver function is acceptable, metformin could be a reasonable choice. Uses of TZDS (for example rosiglitazone and pioglitazone) have also been suggested. These agents have been used for long-term treatment of transplant induced diabetes mellitus with some success in combination with other agents (for example sulphonylureas or insulin)

Insulin can be used safely and effectively in patient with glucocorticoid induced hyperglycemia. Two general approaches have been advocated. The first focuses on prandial insulin therapy. The basis for this strategy appears to be the observation that, whereas fasting glucose concentrations are typically normal when glucocorticoids are administered once daily, glucose levels increase after breakfast and particularly after lunch, with a gradual decline toward normal overnight. The rise in glucose concentrations throughout the day has then been interpreted as evidence for a specific defect in postprandial insulin secretion which should be addressed by prandial insulin.

An alternative strategy is suggested based on the known effect of weight and glucocorticoid dose on insulin sensitivity. It is well recognized that as body weight (and body fat) increases, insulin resistance also increases. NPH insulin is chosen for glucocorticoid induced hyperglycemia because of the time course of action shown in available pharmacodynamic data. Just as prednisolone and prednisone have a peak action at 4 to 8 hours and a duration of 12 to 16 hours, NPH insulin has a similar action profile. A suggested weight based algorithm for insulin based on the known

dose response effects of glucocorticoid on insulin sensitivity is suggested. The insulin doses are averages and may necessitate individual adjustment.

The advantages of this strategy are many. First it is simple. A single administration of insulin is required for most patients and the titration schedule can be easily explained. Second it is proactive. Third it reinforces the critical role of patients in their own glucose management at a time when dramatic glucocorticoid induced increases in glucose values might otherwise lead to frustration.

Several studies revealed that post prandial hyperglycemia including impaired glucose tolerance is a risk factor for mortality and is closely associated with cardiovascular disease. In addition authors of another study found that acute hyperglycemia (>270 mg/dl) induced significant increases in platelet aggregation and blood viscosity, which are regarded as important cardiovascular risk factors. And Glucocorticoid induced diabetic ketoacidosis has been reported.[56].

Pulse therapy means the administration of large (Supra – pharmacologic) doses of drugs in an intermittent manner to enhance the therapeutic effect and reduce the side effects.

The first reported use of pulse administration of corticosteriods is attributed to Kountz and Cohn who used it successfully prevent renal graft rejection. Subsequently pulse doses of corticosteroids were used for several other disease such as lupus nephritis, rheumatoid arthritis and pyoderma gangrenosum,. But usually to deal with emergency situations only and not as a preferred method of treatment. Methyl prednisolone was the commonest drug used, in a dose of 1g per dose for a variable number of days. For pemphigus the pulse therapy was first used by Pasricha in 1982,

for systemic sclerosis in 1989, for pyoderma gangrenosum in 1990 and other diseases in subsequent years.

The pulse therapy region designed by Pasricha et al is called DCP regimen or the Dexamethosone cyclophosphamide pulse (DCP) therapy regimen. In its present form, it consists of giving 100 mg dexamethasone dissolved 1n 500 ml of 5% glucose as a slow intravenous drip over 2 hours repeated on 3 consequent days. On the second day the patient is also given 500 mg cyclophosphamide in the same drip. This constitutes one DCP such DCps are repeated at exactly 28 day intervals counted from the day first of the pulse. In between the pulse patient receives only 50 mg cyclo phosphamide orally per day. The DCP regimen is administered in four phases. During the first few months (phase I) the patient may continue to develop recurrences of clinical lesions in between the DCPs and can therefore be given additional treatment (conventional daily doses of oral corticosteroids or additional dexamethasone pulses) to achieve quicker clinical recovery and these are as a rule withdrawn stepwise during the subsequent DCPs. After the skin and the mucous membrane lesions have subsided completely and the additional medication has been with drawn, the patient is considered to have entered phase II. During this phase, the patient remains completely alright clinically but receives 9 more DCPs at exactly 28 days cycles along with 30 mg cyclophosphamide orally per day. During the next phase (phase III). The DCPs are stopped and the patient receives only 20mg cyclophosphamide orally per day for the next 9 months. After this the treatment for pemphigus is withdrawn completely and the patient is followed up for the next 10 years to took for a relapse in any (phase IV).

Contraindications

There are almost no contraindications. DCP therapy can be given to patients of all ages but the doses have to be reduced to half for children below the age of 12 years. It can also be given to patients having diabetes mellitus, hypertension, hyperacidity, osteoporosis, tuberculosis etc. but each patient must receive additional appropriate treatment for the concomitant disease whenever necessary. Diabetic patients need to be given 10 units of soluble insulin for every 500 ml bottle of 5 % glucose dissolved in the same drip in addition to the routine treatment for diabetes. If the patient has severe infected lesions or those is a serious infection elsewhere the start of the pulse therapy can be delayed for a week or two till the infection has been brought under control.

The only contraindication for pulse therapy is pregnancy or if the patient is a lactating mother and feeding her infant. Patients who are unmarried or those who have not yet completed their family and want to have more children have to be given only Dexamethasone pulses (DPs).

Side effects

The major adverse effects seen. Particularly in the first two phases were increased susceptibility to infections for example, secondary bacterial infection of the lesions. Oral candidiasis, widespread tinea and the reactivation of dormant tuberculosis. The other major side effects were amenorrhea in women, azoospermia in men and hair loss. The main advantages of DCP were the quick healing of lesions and absence of side effects of corticosteroids (eg: weight gain, diabetes and osteoporosis).

The commonest immediate side effects of DCP is flushing, followed by the more delayed ones like generalized weakness and inadequate sleep syndrome. Irreversible amenorrhoea has been noted. Other side effects included a feeling of weakness and tiredness due to corticosteroids withdrawl for 2-3 days after the pulse, bad taste in the mouth and loose motions coinciding with the pulses. Recurrent hiccups after the pulse, cataract, bone pain with similar intention as DCP regimen oral minipulse with steroids like Betamethasone, prednisolone and methyl prednisolone has been tried in various condition. Its chief aim is to provide maximum efficacy and to minimize the side effects of steroids.

In a study conducted on alopecia patients where the patients treated with Betamethasone oral minipulse therapy, they concluded that the oral minipulse therapy is a safe and effective treatment modality for extensive alopecia areata[4].

Similarly prednisolone oral mini [pulse therapy has been tried in treatment of alopecia areata with success. They concluded that the therapy is a convenient and effective therapy for the treatment of extensive alopecia areata of recent onset [5.]

In a study on a vitiligo patients, they treated the patients with low dose predinisolone and they concluded that low dose predinisolone is an effective method in preventing progression and inducing regimentation of rapid spreading vitiligo without serious side effects.

In another study of childhood vitiligo involving four hundred children treated with oral methyl predinisolone on two consecutive days every week in a minipulse form for a period of six months with more than 90 % patients went into complete remission [6].

Materials & Methodology

MATERIALS AND METHODS

A. Inclusion Criteria

Patients with alopecia areata, vitiligo, lichen planus were included

B. Exclusion Criteria

Patients with diabetes mellitus, associated infections, pregnant women were excluded from the study.

Total of 22 patients were studied. The study was conducted over a period of 12 months at the Department of Dermatology, Venereology and Leprology, PSG Hospitals, Coimbatore, Tamil Nadu.

Patients were hospitalized for 2 days. On the first day, baseline fasting blood sugar was done and 2 hours later post prandial blood sugar was done.

Estimation of Blood sugar

The estimation of blood sugar was done by calorimetric method. The values were calculated in mg/dl. The normal fasting blood sugar and post prandial blood sugar levels were 70 – 110 mg/dl and <140 mg/dl, respectively.

On day 2 methylpredinisolone 1.7 mg/kg was administered to the patients as a single morning dose and patients had breakfast. After 2 hours post – prandial blood sugar was measured by calorimetric method.

The results were tabulated

Details of hyperglycemic symptoms were noted in the last 10 patients since a patient started on oral steroid minipulse had developed hyperglycemic symptoms(dryness of mouth).

The presence or absence of the following hyperglycemic symptoms were noted:

Increased frequency of urination

Excessive thrist

Dehydration – Dry mouth

Nausea, vomiting

Fatigue

Confusion

Lack of Concentration.

STATISTICAL ANALYSIS

Data were analyzed by paired “t” test.

Data were expressed as mean.

The chosen level of significance was $p<0.05$.

Results & Analysis

RESULTS

A total of twenty two patients were studied. The age of the patients ranged between 12 years and 56 years with a mean age of 31.18 years. Of the twenty two patients eight were men and fourteen were women. Out of the twenty two patients nine patients were diagnosed with Vitiligo, ten patients with alopecia areata, one patient with Lichen planus and two patients with chronic severe pruritus.

The mean value of the fasting blood sugar (83.51) and post- parandial blood sugar before and after giving oral methyl prednisolone (112.77 and 112.40 respectively) is shown in Table 1.The statistical analysis is shown in Table 2.

The details of hyperglycemic symptoms which were noted in the ten patients is shown in Table 3. The mean value of post prandial blood sugar before and after giving steroid was 112.77 mg/dl and 142.41 respectively. The difference was statistically significant (P value was 0.000782).

The standard deviation of the fasting blood sugar, post prandial blood sugar levels (7.04, 21.66 and 31.23 respectively) showed that there is a wide range of post - prandial blood sugar levels after giving oral methyl predinisolone. Out of ten patients who were enquired about hyperglycemic symptoms two patients had excessive thirst and two had symptoms of dehydration like dry mouth.

Table – 1

Mean Value of Fasting & Post prandial blood sugar before & after giving steroid

Fasting Blood Sugar	Before Steroid	After Steroid
83.54545	112.7727	142.4091

Table - 2

Statistical Analysis

	Mean	S.D	T Value	P Value
FBS & PPBS Presteroid	83.54545 112.7727	7.042235 21.6615	6.1449	0.000004263
FBS & PPBS Post steroid	83.54545 142.4091	7.042235 31.23743	8.2709	0.00000004808
PPBS Presteroid & PPBS Post steroid	112.7727 142.4091	21.6615 31.23743	7.9595	0.00000008933

Table - 3

Details of Hyperglycemic Symptoms

Hyperglycemic Symptoms	No of Patients.
Increased frequency of urination	-
Excessive thirst	2
Dehydration – dry mouth	2
Nausea	0
Vomiting	0
Other Symptoms	0

Discussion

DISCUSSION

Steriods are commonly used in autoimmune disease like pemphigus[57], Bullous pemphigoid, Alopecia areata, Vitiligo and other dermatological diseases. Pulse therapy with supra pharmacological doses of steroids is effective and it is associated with fewer side effects than conventional doses of steriods [57,] the exact mechanism of pulse therapy is not known and postulated to be due to sequestration of lymphocytes[58]. Intravenous Dexamethasone in the form of Dexa methasone cyclophosphamide pulse therapy has been proved success in the treatment of various disorders like pemphigus[57]. Its chief aim is to provide maximum efficacy with minimal side effects.With similar intention, oral minipulse in the form of betamethasone or methylpredinisolone has been used in alopecia areta, vitiligo patients [3, 4, 5].

Oral minipulse may be used for a longer periods with minimal side effects when compared to daily doses of corticosteroids. Systemic corticosteroids has been associated with side effects like hypertension, hyperglycemia, eye changes like cataract and glaucoma, electrolyte imbalance and bone changes like osteoporosis and vascular necrosis.

Corticosteroids stimulate glycogenolysis and gluconeogenesis and increased peripheral insulin. resistance theraby leads to hyperglycemia [59]. The pattern of steroid induced hyperglycemia is post prandial hyperglycemia [59], but does not effecting fasting blood sugar levels.

In our study there was a significant rise in post prandial blood sugar after giving oral methylprednisolone pulse. The standard deviation of fasting blood sugar,

post prandial blood sugar before and after steroids (7.04, 21.66 and 31.23 respectively) showed that there is a wide range of post prandial blood sugar values after giving oral steroids.

In one study conducted in 25 patients with neurological disease treated with prednisolone 30 mg/daily, thirteen patients developed steroid induced diabetic mellitus following steroid therapy for more than 2 weeks. [59]

In another study involving patients with rheumatoid arthritis on corticosteroids therapy 8 % of the non – diabetic patients developed diabetes mellitus and 6 patients with Diabetes in whom glycemic control worsened.[42]

In yet another study which was a retrospective review of pateients hospitalized for various conditions over one month period in those receiving steroids, hyperglycemia was documented in 32 of 50 patients and multiple hyperglycemia episodes occurred in 26 (52%). Among patients without a history of diabetes 19 of 34 (56%) had hyperglycemia at least once.[6]

Life threatening complication like steroids induced diabetic ketoacidosis has been reported[56]. We initiated this study since one of our patient who was on methylprednisolone pulse therapy for vitiligo met with an accident following which his blood sugar increased more than 450mg/dl and emergency measures were required to reduce the blood sugar levels.Hyperglycemic symptoms were observed in four out of ten patients (40%). Out of those four patients PPBS was more than 190 mg/dl in two patients and the other two patients had PPBS more than 140 mg/ dl. This showed that the hyperglycemic symptoms were common in patients with high Blood sugar levels.

Conclusion

CONCLUSION

We suggest that all the patients treated with either steroid pulse or oral minipulse should undergo fasting blood sugar and post prandial blood sugar before and after steroids.

And the physician should be alert regarding the symptoms associated with hyperglycemia.

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Annexures

MASTER CHART

S. No	Name	Sex	Age	FBS	PPBS	PPBS
1	Arul Kumar	M	26	95	101	132
2	Elakkiya	F	18	98	115	136
3	Sathya	F	21	84	92	117
4	Saraswathy	F	24	77	122	167
5	Thayammal	F	51	97	107	131
6	Kalimuthu	M	56	84	166	174
7	Malathi	F	26	81	96	116
8	Bhagavathy	F	33	74	132	198
9	Dhanabhagyam	F	38	89	152	178
10	Eswari	F	24	83	99	136
11	Gunesekaran	M	31	78	120	168
12	Gopalasundaram	M	35	83	125	165
13	Kalai Selvi	F	17	86	113	121
14	Pappathy	F	49	95	126	144
15	Sangeetha	F	12	82	97	100
16	Veeraiyan	M	53	80	88	96
17	Priyadharshini	F	21	77	138	201
18	Kumar	M	27	82	94	121
19	Selvi	F	25	80	88	104
20	Thilaga	F	32	79	126	174
21	Palanisamy	M	43	78	86	112
22	Mani	M	48	76	98	142
	Total			83.54545	112.7727	142.4091